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OBESITY AND GYNECOLOGICAL MALIGNANCIES: A MULTI-CENTRIC CROSS SECTIONAL STUDY

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ABSTRACT **Introduction**: Obesity is a growing problem and has significant implications for a variety of diseases, including human cancers. Obesity has now become an epidemic so is the increase of gynecological malignancies in this era. So we review the association of obesity and gynecological malignancies like breast, endometrial, cervical, ovarian, tubal and Vulvo-vaginal carcinoma as an independent etiological risk factor. **Aims and objectives:** To estimate the prevalence of overweight and obese female in western Indian population. To find the association of different gynecological malignancies and obesity. To evaluate the effect of obesity on different gynecological malignancies in accordance with age, reproductive life and socioeconomic status. **Materials and methods:** A cross sectional study in western Indian states Gujarat, Maharashtra and Rajasthan from January 2019 to December 2021, 10245 sample size and with overweight and obese post menarchal women up to 70 years of age with BMI >25 kg/m2 were compared to matched controls. All the consented subjects were initially screened by questionnaire by field worker and examined for routine and advanced screening and examinations like Manual Palpation of breast, per abdomen, per speculum per vaginal examination and Pap smear by certified professionals according to standard protocols. Investigation was performed when required like mammography, Ultrasonography and laboratory investigations. **Results:** Positive association of breast and endometrial carcinoma especially in postmenopausal women and cervical carcinoma. Weak positive association for ovarian carcinoma only in premenopausal woman (not statistically significant). We do not find enough cases to conclude anything for vulvo vaginal and tubal carcinoma. **Conclusion:** Growing epidemic of obesity can be statistically correlated with increasing incidence of gynecological malignancies like breast, endometrial, ovarian and cervical. Large scale studies further needed for evaluation of correlation of vulvo vaginal and tubal carcinomas.

INTRODUCTION:

Obesity rates swell in India: One-fifth of Indian women are now overweight. According to the National Family Health Survey (NFHS-4), one-fifth of Indian women, or 20.7 per cent to be precise, in the age group of 15-49 are overweight.[1] Worldwide, obesity has more than tripled since 1975, according to the World Health Organization (WHO).[2] Overweight and obesity are linked to more deaths worldwide than underweight and normal weight. Generally, obesity is caused by sedentary lifestyles – physical inactivity, unhealthy diet and eating habits.

Being obese puts you at a higher risk of developing a number of potentially serious health problems, including – heart disease, stroke, diabetes, breathing disorders, musculoskeletal disorders (especially osteoarthritis), gallbladder disease, pregnancy related complications, infertility, non-alcoholic fatty liver disease, kidney disease and some cancers.

A body mass index (BMI) > 30 is associated with increased risk for many female cancers, including endometrial, gallbladder, esophageal, renal, leukemia, thyroid, and breast cancers. Obesity also increases cancer-related morbidity and mortality.

There is increasing awareness of the effect obesity also may have on cancer, as new evidence suggests that overeating along with obesity may be the largest preventable causes of cancer among nonsmokers and may account for one in five cancer deaths among women. A higher BMI leads to a worse outcome in cancer patients.

Women with obesity may have shorter survival secondary to delay in cancer screening or suboptimal dosage of chemotherapy. Several mechanisms have been proposed to link the association between obesity and cancer promotion including insulin resistance, estrogen, adiposity, and low-grade chronic inflammation.

Endometrial carcinoma: Several risk factors have been proposed, including postmenopausal unopposed estrogen use, nulliparity, diabetes mellitus, and obesity. Obesity has been estimated to account for up to 40% of endometrial cancer incidence in developed countries.

Cervical carcinoma: The incidence of and mortality from cervical cancer have decreased with the advent of the Papanicolaou test for cervical cancer screening. A meta-analysis review suggested that obese women were less likely to report being screened for cervical cancer than their lean counterparts. Less screening may partly explain the higher cervical cancer mortality seen in obese women. Cervical adenocarcinoma was found to be strongly associated with obesity rather than squamous cell carcinoma.

Ovarian carcinoma: Ovarian cancer is a highly fatal disease, with only 40% of women with ovarian cancer alive >5 years after diagnosis. One of the reasons contributing to the poor prognosis of ovarian cancer is that approximately 75% of patients with ovarian cancer receive a diagnosis of metastatic spread beyond the pelvis.

The rationale for increased risk of ovarian cancer in women with obesity focuses on the hormonal effect of obesity. A 30%

increased risk of ovarian cancer in obese women (BMI of >30 kg/m2) has been reported from a meta-analysis. It has been hypothesized that in menopausal women, adiposity enhances ovarian cancer risk partly through the mitogenic effects of excess endogenous estrogen synthesized in the adipose tissue.

Breast Carcinoma: There is growing evidence to link between obesity and breast cancer. For postmenopausal women, prospective cohort studies have associated increasing BMI with increasing breast cancer incidence in postmenopausal women, especially in those with hormone-positive breast cancer. A meta-analysis estimated overweight or obese was associated with a 78-91% increased risk of recurrence and a 36-56% increased risk of death in women with breast cancer.

AIMS AND OBJECTIVES:
- To estimate the prevalence of overweight and obese female in western Indian population.
- To find the association of different gynecological malignancies and obesity.
- To evaluate the effect of obesity on different gynecological malignancies in accordance with age, reproductive life and socioeconomic status

MATERIALS AND METHODS:
For the present study, post menarchal women aged 15-70 years in urban and rural areas were considered. The analysis is based on the economic stratum. This multi-centric randomised cross-sectional study was conducted after consenting all the subjects from various urban and rural female populations.

Total 10245 subjects were taken in to this study according to their age, economic status, obstetric status, caste, menstrual level and various other parameeters.

Outcome variables
Overweight and obesity
All women aged 15-70 years were weighted using digital weighing scale which was calibrated to $\pm$ 100 Gms.

Their heights were measured using adjustable wooden measuring board specifically designed to measure accurate measurements nearest up to 0.1 cm. Kit (height and weight machines) were provided to all co investigators and field workers.

As per definition of WHO,
Normal range of BMI (18.5-24.9)
Under weight (less than 18.5 kg/m2)
Over weight (25-29.9)
Obese grade 1 (30-34.9)
Obese grade 2 (35-39.9)
Morbid obese. (More than 40)

Based on these cut-offs, the present study uses two category variables of nutritional status of women, merging underweight and normal to indicate "not obese" and remaining all overweight and obese indicate "obese".

The survey collected information on number of demographic and socioeconomic factors which could potentially affect the nutritional status of the women. The variables which are included in this study for analysis are age of respondent, religion, caste, educational attainment, marital status, parity, exposure to media.

- A Randomized Multi-centric Cross sectional study of 10245 consented subjects in 10 different geographical areas of Gujarat, Rajasthan and Maharashtra from urban, semi urban and rural area

- Duration of the data collection was 36 months between 1 January 2019 to 31 December 2021.
- Inclusion criteria
- All consented post menarchal women
- Post menarchal to age of 70 years.
- Exclusion criteria
- Bed ridden patients
- Not able to give consent
- Minors whose guardians are not willing
- Primary amenorric patients with proven cause
- Those lost to follow up.

Study instruments:-
- Pre tested and Piloted
- Mostly fully close ended questionnaire
- Few open ended questionnaire

Method of Data Collection:
Personal Interview by field worker and doctor.

Personal interview and clinical examination by co investigator.

Data entry
- Mostly by C S Pro software
- Few by Microsoft excel

Data Analysis
- SPSS
- Microsoft excel
- Social Science Statistics
- **Data analysis by**
- 1. Frequency
- 2. Association
- 3. Multinomial logistic Regression analysis
- 4. Relative Risk Ratio

OBSERVATIONS AND RESULTS:
Table 1- age wise distribution of obese and non obese subjects

Age	Obese	Non obese	Total
10-18	201	882	1083
18-35	660	2866	3526
35-50	826	2506	3332
>50	975	1329	2304
Total	2662	7583	10245

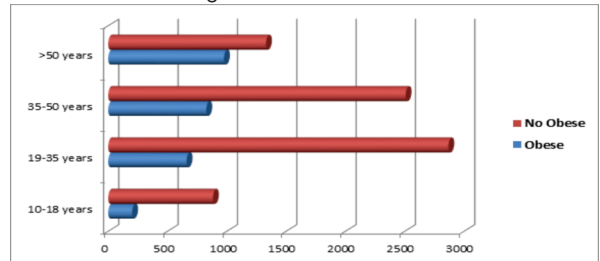According to our study, prevalence of the obesity was 26 % which increases as age increases.

Table 2- Total Malignancy with obesity

Malignancy→ Obesity ↓	Yes	No	Total
Yes	33	2629	2662
No	20	7563	7583
Total	53	10192	10245

There is highly statistical significant observed difference between Obesity & malignancy the chi-square statistic is 36.4633. The p-value is < 0.00001. Significant at 95% confidence level & 1 degree of freedom.

We found total 53 patients of gynecological malignancies in our study population. So prevalence of overall gynecological

malignancies is 0.5% in our study.

Out of 53, 33 (62%) patients are obese and 20 (38%) are non obese. There is strong correlation found between obesity and gynecological malignancies using chi square test.

Table-3 Age wise distribution of malignancy

Age	malignant	Non malignancy	Total
10-19	0 (0)	1083	1083
19-35	11 (0.1)	3515	3526
35-50	30 (0.3)	3302	3332
>50	12 (0.1)	2292	2304
Total	53 (0.5%)	10192	10245

The prevalence of malignancy is 0.5% in our study. Highest number of malignancies is seen in age group of 35-50 years.

Table 4 - Reproductive/Sexual Life Wise distribution of obesity

	obese	Non obese	Total
Menarche to Active sexual life	202	1097	1299
Active Sexual life to Menopause	1282	4906	6188
Post menopausal	1178	1580	2758
Total	2662	7583	10245

A chi-square test of independence was performed to examine the relation between reproductive/sex life with obesity. The relation between these variables was significant, X^2 (2, N = 10245) = 564, p = 0.00005.

Table 5 - Reproductive/Sexual Life Wise distribution of malignancy.

Age	Malignant (%)	Non malignant (%)	Total
Menarche to Active sexual life	0	1299	1299
Active Sexual life to Menopause	34	6154	6188
Post menopausal	19	2739	3332
Total	53	10192	10245

Prevalence of malignancy was observed higher among those women who are active sexual life rather than post menopausal women.

Highest rate of malignancy is found in middle age women in their reproductive age than post menopausal women.

Table 6 -Type of malignancy (n=53)
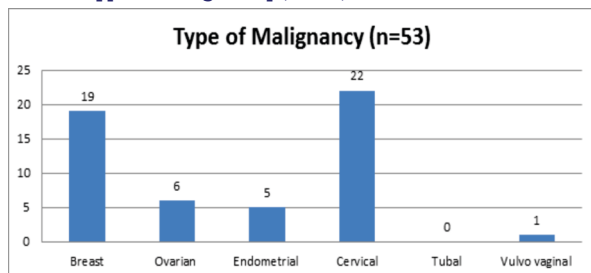
	Obese		Non Obese		
	Malignant	Non Malignant	Malignant	Non Malignant	P value
Breast	13	2649	6	7577	0.000075
Cervical	13	2649	9	7574	0.000393
Ovarian	3	2659	3	7580	0.3809
Endometrial	4	2658	1	7582	0.02477
Vulvo-vaginal	0	2662	1	7582	--
Tubal	0	2662	0	7583	--
Total	33	2629	20	7563	<0.000001

Cervical carcinoma is most common gynecological malignancy observed in our study followed by carcinoma breast. According to our data, the relation between obesity and different gynecological malignancies are statistically significant for breast, cervical and endometrial carcinoma and not significant for ovarian carcinoma. There are not sufficient data obtained from this study for vulvo-vaginal and tubal carcinoma. So need for multi-centric and further large scale study required to get any conclusion for tubal and vulvo-vaginal carcinoma.

Table 7- Age wise distribution of malignancy

	Breast	Ovarian	Endometrial	Cervical	Tubal	Vulvo vaginal	Total
10-18	0	0	0	0	0	0	0
18-35	6	1	0	3	0	1	11
35-50	8	4	2	16	0	0	30
>50	5	1	3	3	0	0	12
Total	19	6	5	22	0	1	53

Breast, ovarian and cervical carcinoma are more commonly seen in active reproductive age group while endometrial carcinoma is more seen with postmenopausal age group.

Table 8 - According To Kuppuswamy Classification

	Upper		Middle		Lower Middle		Upper Lower		Lower		
	obese	Non obese	Obese	Non obese	obese	Non Obese	obese	Non Obese	obese	Non Obese	Total
Breast	5	1	3	1	2	1	2	2	1	1	19
Cervical	2	1	2	0	1	0	4	2	4	6	22
Ovarian	1	0	0	1	0	0	1	0	1	2	6
Endo	0	0	2	0	1	0	0	1	1	0	5
Vulvo-vaginal	0	0	0	0	0	0	0	1	0	0	1
Tubal	0	0	0	0	0	0	0	0	0	0	0
Total	8	2	7	2	4	1	7	6	7	9	53
Total	10	9	5	13	16	53					

In this table there is distribution of gynecological malignancies with obesity according to kuppuswamy socio economic classification.

Breast cancer is more seen upper and middle income groups while cervical cancer is more seen in lower and lower middle income groups, suggesting the role of environmental factors, poor hygiene and infective etiologies. Fewer trends to visit to any medical doctor after first symptoms also play an important role.

SUMMARY:
After this study we have found that more prevalence (25.98 %) of the overweight and obese female population in society than recorded in National Family health survey 4 and 5. This prevalence of overweight and obesity is increasing significantly in our country. Obesity is seen as a growing epidemic in the world which causing significant health hazards towards mankind especially in women.

Positive association of obesity and breast carcinoma and endometrial carcinoma especially in postmenopausal women and cervical carcinoma is found.

Obese women were less likely to report being screened for

cervical cancer than their lean counterparts. Less screening may partly explain late diagnosis and the higher cervical cancer mortality seen in obese women.

The higher risks breast cancers are seen mainly in women who have never used menopausal hormone therapy and for tumors that express receptors. In premenopausal women, by contrast, overweight and obesity have been found to be associated with decreased risk of breast tumors that express hormone receptors.

Weak positive association of obesity with ovarian carcinoma only in premenopausal woman (not statistically significant) is found.

There are not sufficient data obtained from this study for vulvo-vaginal and tubal carcinoma. So need for multi-centric and further large scale study required to get any conclusion for tubal and vulvo-vaginal carcinoma.

CONCLUSION:

Obesity has become an emerging challenge in human diseases including malignancy. However, it is not surprising that in no circumstance was obesity found to exert a positive benefit. With increasing evidence of the effect of obesity in gynecological malignancy, the better approach to prevent and manage obesity related gynecological malignancy should be addressed in the future.

With this backdrop the growing demand which appears before Government or health planners is to address this rising epidemic with equal importance. A timely intervention will reduce the burden of many chronic and acute co morbidities like diabetes, cardiovascular diseases, hypertension, cancers, infertility, depression and many pregnancy related complications. This can be achieved either through undertaking separate urban health programme or incorporating special clause in proposed national health programme or in CSR activity, citing the importance of healthy diet and physical exercise.

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